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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/684,305	10/06/2000	Michael W. Kaiser	FORS-04447	5698
72960	7590	12/01/2011		
Casimir Jones, S.C. 2275 DEMING WAY, SUITE 310 MIDDLETON, WI 53562			EXAMINER	
			STAPLES, MARK	
			ART UNIT	PAPER NUMBER
			1637	
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			12/01/2011	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 09/684,305	<b>Applicant(s)</b> KAISER ET AL.	
	<b>Examiner</b> MARK STAPLES	<b>Art Unit</b> 1637	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 09 September 2011.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on \_\_\_\_; the restriction requirement and election have been incorporated into this action.
- 4) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 5) ☒ Claim(s) 53-108 is/are pending in the application.
- 5a) Of the above claim(s) 65-81 and 98-105 is/are withdrawn from consideration.
- 6) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 7) ☒ Claim(s) 53,56-64,82-95 and 106-108 is/are rejected.
- 8) ☒ Claim(s) 54,55,96 and 97 is/are objected to.
- 9) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 10) ☐ The specification is objected to by the Examiner.
- 11) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 12) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)          | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. ____.                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date ____.  | 6) <input type="checkbox"/> Other: ____.                          |

### **DETAILED ACTION**

1. Applicant's amendment of claims 53, 54, 56, 95, 96, 103, and 104 in the paper filed on 09/09/2011 is acknowledged.

Claims 53-64, 82-97, and 106-108 consonant with species elections are pending and at issue.

#### **Terminal Disclaimer**

2. The terminal disclaimer filed on 11/02/2011 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of U.S. Patent No. 5,843,669 has been reviewed and is accepted. The terminal disclaimer has been recorded.

The double patenting rejection over U.S. Patent No. 5,843,669 is withdrawn.

#### **Objections and Rejections that are Withdrawn**

3. Objections and rejections not reiterated herein are hereby withdrawn.

#### **Rejections that are Maintained**

##### ***Claim Rejections Maintained - 35 USC § 103***

4. The rejection of claims under 35 U.S.C. 103(a) as being unpatentable is maintained. Applicant's arguments have been fully considered but they are not persuasive. The full rejection is re-provided below.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., the nucleic acid substrate is "DNA" and is not "RNA") are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). And thus the teaching of Thompson et al. of an archaeal and bacterial enzyme with RNA nucleic acid substrates reads on the claims.

In regards to Applicant's argument concerning Wu et al. confirms that both human and bacterial RAD2 enzymes function as FEN-1 enzymes as claimed: "In all eukaryotic cells, an enzyme called FEN-I . . . appears to function as both a 5' flap DNA endonuclease and a ds DNA 5'-exonuclease (1,2). This 42 kDa endo-/exonuclease, FEN-I, has been shown to be highly homologous to human XP-G, *Saccharomyces cerevisiae* [bacterial] RAD2 and *Scerevisiae* RTHI (3). These structure-specific nucleases recognize and cleave a branched DNA structure called a DNA flap, and its derivative called a pseudo V-structure (4)" (see 1<sup>st</sup> paragraph under the *Introduction* on p. 2036).

The combined teachings thus provide reasonable expectation that the methods using archaeal enzymes and nucleic would have been successful. It would also have been obvious at the time of the claimed invention to substitute an archaeal enzyme for the a human enzyme to form one or more cleavage structures, from both the teaching of Wu et al. and Thompson et al.

*Claim Rejections Maintained- 35 USC § 103*

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 53, 56-64, 82, 83, 85-95, and 106-108 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wu et al. (June 11, 1996), Thompson et al. (1988), and Zhang et al. (1992).

The claims are directed to processes using archaeal endonucleases to cleave nucleic acids. There are no pending product claims.

Regarding claims 53, 56, 60-62, 82, 85-90, 106, and 107 Wu et al. teach methods for treating nucleic acid, comprising: a) providing:

- i) a purified FEN-1 endonuclease (see 2<sup>nd</sup> paragraph on p. 2042); and
- ii) a single stranded DNA nucleic acid substrate (see Abstract and 2<sup>nd</sup> paragraph on p. 2042) which single strand from double stranded DNA can be created by the endonuclease tracking along a single-strand DNA branch/oligonucleotide which is not hybridized and thus is not complementary to the target nucleic acid (see Abstract) , or where with use of PCNA a double stranded DNA may be used (see Abstract);
- b) treating said nucleic acid substrate under conditions such that said substrate forms one or more cleavage structures (see 2<sup>nd</sup> paragraph on p. 2042); and
- c) reacting said endonuclease with said cleavage structures so that one or more cleavage products are produced (see 2<sup>nd</sup> paragraph on p. 2042).

Regarding claim 53, Wu et al. do not specifically teach an archaeal FEN-1 endonuclease.

Regarding claims 56-58 and 92-94, Wu et al. teach use of polymerase thermostable at the temperature of cleavage (see 2<sup>nd</sup> paragraph on p. 2042) including eukaryotic polymerases (see Abstract) and *E coli* polymerases (see last sentence on p. 2019).

Further regarding claims 56-58 and 92-94, that *Thermus aquaticus* DNA polymerase was well known in the prior art for use with endonuclease is found in the methods and applications of Bej et al. (see section 2 on p. 302 and first full paragraph on p. 305).

Regarding claim 63, Wu et al. teach the double strand melts (see legend to Figure 7) that is, denatures due to temperature.

Regarding claim 64 and 91, Wu et al. detecting cleaved products (see Figure 8). It is noted that the method of Wu et al. is repeatable can generate second cleavage products. Repetition of a process is routine.

Regarding claims 53, 95 Thompson et al. teach archaeal FEN-1 endonucleases from *Halobacterium volcannii* (see Title).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the methods of cleaving nucleic acids using eukaryotic endonucleasases of Wu et al. to substitute an archeal FEN-1 endonucleases from *Halobacterium volcannii* for the eukaryotic endonuclease as suggested by Thompson et al. with a reasonable expectation of success. The motivation to do so is provided by Thompson et al. who teach: "Cleavage of the phosphodiester bonds occurred in a manner analogous to that observed for the eukaryotic tRNA intron endonuclease . . ." ( see last full paragraph on p. 17954). Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

Regarding claim 108, Zhang et al. teach methods of cleaving DNA with endonucleases from solid supports (see Abstract and Figures).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the methods of endonuclease cleavage of DNA of Wu et al. and Thompson et al. by cleaving the DNA with an endonuclease from a solid support as suggested by Zhang et al. with a reasonable expectation of success. The motivation to do so is provided by Zhang et al. who teach the use of the solid support permits convenient removal of reagents and catalysts (see Abstract). Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

**New Rejection Prompted by Applicant's Submission**

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).



9. Claims 53, 56-64, 72-75, 77-95, and 106-108 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 4, 5, and 10-40 of copending Application No. 11/489,665. Although the conflicting claims are not identical, they are not patentably distinct from each other because the patent claims recite methods using the species archaeal FEN-1 endonuclease which is *Methoanococcus jannaschii* (Mja) FEN-1 endonuclease which render obvious the genus methods of the instant claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant's submission of the claims of the copending application prompted this rejection.

### **Reference of Interest**

10. Borges et al. (November 2, 1996) is placed in the record as a reference of interest. As with Thompson et al., Borges et al. also teach an archeal FEN-1 endonuclease from archaeal *Pyrococcus furiosus* (see Title and RAD-2, FLAP endonuclease, in Table 1). Borges et al. provide further evidence that archaeal FEN-1 endonucleases of and their function were known at the time of the claimed invention. It is noted that Wu et al. also confirm that human and bacterial RAD2 enzymes function as FEN-1 enzymes: "In all eukaryotic cells, an enzyme called FEN-I . . . appears to function as both a 5' flap DNA endonuclease and a ds DNA 5'-exonuclease (1,2). This 42 kDa endo-/exonuclease, FEN-I, has been shown to be highly homologous to human XP-G,

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*Saccharomyces cerevisiae* [bacterial] RAD2 and Scerevisiae RTHI (3). These structure-specific nucleases recognize and cleave a branched DNA structure called a DNA flap, and its derivative called a pseudo V-structure (4)” (see 1<sup>st</sup> paragraph under the Introduction on p. 2036).

### **Allowable Subject Matter**

11. Claims 54, 55, 96, and 97 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

12. The following is a statement of reasons for the indication of allowable subject matter: no prior art was found which teaches or renders obvious the *Archaeoglobus fulgidus* FEN-1 endonuclease having SEQ ID NO: 179.

13. As allowable subject matter has been indicated, applicant's reply must either comply with all formal requirements or specifically traverse each requirement not complied with. See 37 CFR 1.111(b) and MPEP § 707.07(a).

### **Conclusion**

14. No claim is allowed.

15. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Staples whose telephone number is (571) 272-9053. The examiner can normally be reached on Monday through Thursday, 9:00 a.m. to 7:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Mark Staples/  
Primary Examiner, Art Unit 1637  
November 29, 2011